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EXAMINER	
KAROL, JODY LYNN	
ART UNIT	PAPER NUMBER
1627	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,586	KRUTMANN, JEAN	
	Examiner	Art Unit	
	Jody L. Karol	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/1/2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11 and 14-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 and 14-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of applicant's Amendment/Remarks filed 4/1/2010. Claim 19 has been amended. Claims 1-10 and 12-13 are cancelled. Claims 20-21 are newly added. Claims 11 and 14-21 are pending and currently under consideration.

WITHDRAWN REJECTIONS

1. In view of Applicant's amendment to claim 19, the rejection of claim 19 under 35 U.S.C. 103(a) as being unpatentable over Motitschke et al. (US 6,060,071) in view of Hanifin et al. ("Effects of a Low-potency Corticosteroid Lotion Plus a Moisturizing Regimen in the Treatment of Atopic Dermatitis," *Current Therapeutic Research*, Vol. 59, No. 4, April 1998, pgs 227-233).

MAINTAINED REJECTIONS

2. The following rejections have been maintained from the previous Office Action dated 12/1/2009:

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 11, 14, and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Motitschke et al. (US 6,060,071) in view of Hanifin et al. ("Effects of a Low-potency Corticosteroid Lotion Plus a Moisturizing Regimen in the Treatment of Atopic Dermatitis," *Current Therapeutic Research*, Vol. 59, No. 4, April 1998, pgs 227-233).

The instant claims are directed to a method of treatment of neurodermatitis comprising topical application of a dermatological preparation comprising an osmolyte

or a pharmacologically compatible salt thereof to a patient in need of such treatment, wherein the osmolyte is ectoine or hydroxyectoine or a pharmacologically compatible salt thereof.

It is noted that on page 2 of the instant specification, neurodermatitis is also termed endogenous eczema or atopic dermatitis.

Motitschke et al. teach cosmetic preparations comprising (S)-1,4,5,6-tetrahydro-2-methyl-4-pyrimidinecarboxylic acid (ectoin) and/or (S,S) -1,4,5,6-tetrahydro-5hydroxy-2-methyl-4-pyrimidinecarboxylic acid (hydroxyectoin) for the care of dry and/or irritated skin, in particular for increasing and/or stabilizing the moisture content of skin (see abstract; column 1, line 39 to column 2, line 41; column 6, lines 13-17). The compounds (i.e. ectoin and/or hydroxyectoin) are formulated with auxiliaries and/or carrier substances to give a suitable formulation, wherein examples of use forms include ointments, creams, lotions, sprays, etc. as claimed in instant claim 14 (see column 5, lines 1-13). Motitschke et al. also teach other active substances may be added to the product as claimed in the instant claim 17 (see column 5, lines 13-16). Motitschke et al. further teach that in patients suffering from atopy, the symptoms of dry skin or observed irrespective of age, and that the skin condition can be prevented or counteracted by using suitable moisturizing preparation (see column 1, lines 15-30).

Motitschke et al. do not explicitly teach treating neurodermatitis (atopic dermatitis) using the ectoin and/hydroxyectoin compositions.

Hanifin et al. teach that treatment of atopic dermatitis is directed towards reducing inflammation and using moisturizers to maintain a flexible, hydrated stratum

corneum (see page 228). Hanifin et al. further teach that the addition of a moisturizer to a low-potency topical corticosteroid lotion (i.e. desonide lotion 0.05%, an antiphlogistic and glucocorticoid as claimed in the instant claims 18) in separate regimens was effective in treating the signs and symptoms of mild-to-moderate atopic dermatitis (see abstract). The addition of the moisturizing cream produced significant reduction of up to 23% in the clinical signs and symptoms of atopic dermatitis, which support and overwhelming patient preference for the desonide/moisturizer combination over desonide alone (see pages 231-232, bridging paragraph; page 232 last paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat atopic dermatitis (neurodermatitis) using as moisturizer as taught by Hanifin et al., wherein the moisturizer is the ectoin/hydroxyectoin formulation as taught by Motitschke et al. One of ordinary skill in the art would have been motivated to use the ectoin/hydroxyectoin formulation to treat atopic dermatitis because ectoin/hydroxyectoin formulations improve and stabilize the hydration of the skin. One of ordinary skill in the art would have had a reasonable expectation of success in using the ectoin/hydroxyectoin formulations to treat atopic dermatitis (neurodermatitis) because Motitschke et al. teach that dry skin conditions can be counteracted with said moisturizing preparations, and mention that patients suffering from atopy have dry skin conditions irrespective of age. Further, Hanifin et al. explicitly teach the use of a moisturizer in the treatment of atopic dermatitis.

Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

5. Claims 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Motitschke et al. (US 6,060,071) in view of Hanifin et al. ("Effects of a Low-potency Corticosteroid Lotion Plus a Moisturizing Regimen in the Treatment of Atopic Dermatitis," *Current Therapeutic Research*, Vol. 59, No. 4, April 1998, pgs 227-233). as applied to claims 11, 14, and 17-18 above, and further in view of Touitou et al. ("Liposomes as Carriers for Topical and Transdermal Delivery," *Pharmaceutical Sciences*, Vol. 83, No. 9, Sept. 1994, pgs 1189-1203).

Motitschke et al. and Hanifin et al. are described *supra* as applied to claims 11, 14, and 17-18.

Motitschke et al. and Hanifin et al. do not teach the dermatological preparation comprises liposomes containing the osmolyte (i.e. ectoin, hydroxyectoin, or pharmaceutically acceptable salts thereof).

Touitou et al. teach the advantages of using liposomes as drug carriers for topical delivery, wherein the use of liposomes allows for increased accumulation of the drug in the skin (see abstract; pages 1189-1192, column 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the liposomes taught by Touitou et al. as carriers for the ectoin and/or hydroxyectoin in the method of treating atopic dermatitis obvious over Motitschke et al. in view Hanifin et al. One of ordinary skill in the art would have been motivated to employ liposomes as carriers for the ectoin and/or hydroxyectoin in order to provide the advantages of topical delivery of drugs associated with liposomes, such as the

accumulation of the drug in the skin. One of ordinary skill in the art would have had a reasonable expectation of success in employing the liposomes as carriers for ectoin and/or hydroxyectoin because the method of treating atopic dermatitis obvious over Motitschke et al. in view Hanifin et al. employs a topical composition comprising ectoin and/or hydroxyectoin and Touitou et al. teach the liposomes are drug carriers for topical compositions.

Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

NEW REJECTIONS

6. In light of Applicant's amendments and newly added claims 20-21, the following rejections have been newly added:

7. Claims 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Motitschke et al. (US 6,060,071 in view of Lodén et al. ("Improvement in skin barrier function in patients with atopic dermatitis after treatment with a moisturizing cream (Canoderm®)," *British Journal of Dermatology*, 1999; 140: pgs 264-267).

The instant claims 20 is directed to method of treatment of neurodermatitis comprising topical application of a dermatological preparation consisting essentially of an osmolyte or a pharmacologically compatible salt thereof to a patient in need of such treatment, wherein the osmolyte is ectoine or hydroxyectoine or a pharmacologically compatible salt thereof. The instant claim 21 is directed to a method of treatment of

neurodermatitis comprising topical application of a dermatological preparation comprising ectoine or hydroxyectoine or a pharmacologically compatible salt thereof in the absence of a glucocorticoid.

Motitschke et al. is described *supra* as applied to claims 11 and 14-18.

Motitschke et al. do not exemplify treating neurodermatitis (atopic dermatitis) using the ectoin and/hydroxyectoin compositions.

Lodén et al. teach patients with atopic skin show a defective barrier function in both rough and in clinically normal skin, and that application of a urea-containing moisturizer to the skin of patients with atopic dermatitis improved skin capacitance indicating skin hydration, improved the water barrier function, and reduced skin susceptibility to irritation by sodium lauryl sulphate (see abstract). Lodén et al. further teach that certain moisturizers could improve the skin barrier function in both normal and atopic skin (see page 267).

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat atopic dermatitis (neurodermatitis) using a moisturizer as taught by Lodén et al., wherein the moisturizer is the ectoin/hydroxyectoin formulation as taught by Motitschke et al. One of ordinary skill in the art would have been motivated to use the ectoin/hydroxyectoin formulation to treat atopic dermatitis because ectoin/hydroxyectoin formulations improve and stabilize the hydration of the skin. One of ordinary skill in the art would have had a reasonable expectation of success in using the ectoin/hydroxyectoin formulations to treat atopic dermatitis (neurodermatitis) because Motitschke et al. teach that dry skin conditions, including patients suffering

from atopy, can be counteracted using suitable moisturizing preparations. Further, Lodén et al. specifically teach the use of a moisturizer cream for improving the skin hydration and barrier function in patients with atopic dermatitis.

In regards to claim 21, it is noted that neither Motitschke et al. nor Lodén et al. teach the preparations contain a glucocorticoid.

Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time it was made.

8. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Motitschke et al. (US 6,060,071 in view of Lodén et al. ("Improvement in skin barrier function in patients with atopic dermatitis after treatment with a moisturizing cream (Canoderm®)," *British Journal of Dermatology*, 1999; 140: pgs 264-267) as applied to claims 20-21 above, and further in view of Nghiem et al. ("Tacrolimus and pimecrolimus: From clever prokaryotes to inhibiting calcineurin and treating atopic dermatitis," *J. Am. Acad. Dermatol.*, February 2002, 6(2): pgs 228-241).

The instant claim 19 is directed to a method of treatment of neurodermatitis comprising topical application of a dermatological preparation comprising ectoine or hydroxyectoine or a pharmacologically compatible salt thereof and a calcineurin inhibitor.

Motitschke et al. and Lodén et al. are described *supra* as applied to claims 20-21.

Motitschke et al. and Lodén et al. do not teach compositions containing an active agent that is a calcineurin inhibitor.

Nghiem et al. teach tacrolimus and pimecrolimus, topical inhibitors of phosphatase calcineurin (i.e. calcineurin inhibitors), are useful in the topical treatment of atopic dermatitis (see abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat to treat atopic dermatitis (neurodermatitis) using a ectoin/hydroxyectoin formulation as obvious over Motitschke et al. in view of Lodén et al. in combination with tacrolimus or pimecrolimus as taught by Nghiem et al. One of ordinary skill in the art would have been motivated to combine the ectoin/hydroxyectoin formulation with tacrolimus or pimecrolimus to formulate an effective composition for the treatment of atopic dermatitis. It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose *In re Kerkhoven*, 626 F.2d 846, 205, U.S.P.Q. 1069 (C.C.P.A. 1980). One of ordinary skill in the art would have had a reasonable expectation of success in combining the ectoin/hydroxyectoin formulation as obvious over Motitschke et al. in view of Lodén et al. with tacrolimus or pimecrolimus as taught by Nghiem et al. because each composition is individually taught or obvious over the prior art for the treatment of atopic dermatitis.

Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time it was made.

Response to Arguments

9. Applicant's arguments filed 4/1/2010 have been fully considered but they are not persuasive.

Applicant argues that Hanifin et al. do not disclose that moisturizers alone are effective in the treatment of atopic dermatitis. In response it is respectfully submitted that the "comprising" language of the instant claims 11 and 14-18 is interpreted as broad and open-ended. Thus, the Hanifin et al.'s teaching of a moisturizer plus a corticosteroid is still considered to be applicable to the instant claims 11 and 14-18.

Applicant further argues that Motitschke et al. is deficient because it discloses the use of ectoin and hydroxyectoine only for the treatment of "normal" dry skin and not neurodermatitis. The Examiner respectfully disagrees. Motitschke et al. teach that in patients with atopy, the symptoms of dry skin are observed irrespective of age, and that this skin condition can be prevented as well as counteracted by using suitable moisturizing preparations (see column 1, lines 15-30). Motitschke et al. teach the moisturizing formulations include ectoin/hydroxyectoin improve and stabilize the hydration of the skin (see column 1, lines 39-41). Thus, it is the position of the Examiner that Motitschke et al. is not limited to the use of ectoin and hydroxyectoine for the treatment of "normal" dry skin.

Applicant further argues that an infinite number of compounds have been used as moisturizers and there is no link between the type of compounds capable of curing both dry skin and dermatitis. Applicant further alleges that urea, a well known and effective moisturizer, can not be used for the treatment of atopic dermatitis because it is

not tolerated by patients suffering atopic dermatitis. In response it is respectfully submitted that, as stated *supra*, Motitschke et al. teach that suitable moisturizing preparations can be utilized to treat patients suffering from atopy, wherein moisturizing formulations include ectoin/hydroxyectoin improve and stabilize the hydration of the skin. Further, Applicant provides no evidence that other moisturizers, i.e. urea, are ineffective in the treatment of atopic dermatitis. The arguments of counsel cannot take the place of evidence in the record. *In re Schulz*, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 43 USPQ2d 1362 (Fed. Circ. 1997) ("An assertion of what seems to follow from common experience is just an attorney argument and is not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness.")

Thus, for these reasons, Applicant's arguments are found unpersuasive. Said rejection is maintained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jody L. Karol whose telephone number is (571)270-3283. The examiner can normally be reached on 8:30 am - 5:00 pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

/Jody L. Karol/

Examiner, Art Unit 1627

/Yong S. Chong/
Primary Examiner, Art Unit 1627